Abstract

The NG108-15 neuroblastoma / glioma hybrid cell line has been frequently used for toxin detection, pharmaceutical screening and as a whole-cell biosensor. However, detailed analysis of its action potentials during toxin or drug administration has not been accomplished previously using patch clamp electrophysiology. In order to explore the possibility of identifying toxins based on their effect on the shape of intracellularly or extracellularly detected action potentials, we created a computer model of the action potential generation of this cell type. To generate the experimental data to validate the model, voltage dependent sodium, potassium and high-threshold calcium currents, as well as action potentials, were recorded from NG108-15 cells with conventional whole-cell patch-clamp methods. Based on the classic Hodgkin-Huxley formalism and the linear thermodynamic description of the rate constants, ion-channel parameters were estimated using an automatic fitting method. Utilizing the established parameters, action potentials were generated in the model and were optimized to represent the actual recorded action potentials to establish baseline conditions. To demonstrate the applicability of the method for toxin detection and discrimination, the effect of tetrodotoxin (a sodium channel blocker) and tefluthrin (a pyrethroid that is a sodium channel opener) were studied. The two toxins affected the shape of the action potentials differently and their respective effects were identified based on the changes in the fitted parameters. Our results represent one of the first steps to establish a complex model of NG108-15 cells for quantitative toxin detection based on action potential shape analysis of the experimental results.

Keywords: Action potential shape analysis, Toxin detection, NG108-15, Computer simulation, Linear thermodynamic model, Hodgkin-Huxley model